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PAPER

Assessment of alginate hydrogel degradation in biological tissue using viscosity-sensitive fluorescent dyes

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Abstract

The main goal of this study is to investigate a combination of viscosity-sensitive and viscosity-insensitive fluorescent dyes to distinguish different rheological states of hydrogel based biostructural materials and carriers in biological tissues and to assess their corresponding location areas. The research is done in the example of alginate hydrogel stained with viscosity-sensitive dyes **Seta-470** and **Seta-560** as well as the viscosity-insensitive dye **Seta-650**. These dyes absorb/emit at 469/518, 565/591 and 651/670 nm, respectively. The rheological state of the alginate, the area of the fluorescence signal and the mass of the dense alginate versus the calcium gluconate concentration utilized for alginate gelation were studied *in vitro*. The most pronounced change in the fluorescence signal area was found at the same concentrations of calcium gluconate (below ~1%) as the change in the alginate plaque mass. The stained alginate was also implanted *in situ* in rat hip and myocardium and monitored using fluorescence imaging. In summary, our data indicate that the viscosity sensitive dye in combination with the viscosity-insensitive dye allow tracking the biodegradation of the alginate hydrogel and determining the rheological state of hydrogel in biological tissue, which both should have relevance for research and clinical applications. Using this method we estimated the half-life of the dense alginate hydrogel in a rat hip to be in the order of 4 d and about 6–8 d in rat myocardium. The half-life of the dense hydrogel in the myocardium was found to be long enough to prevent aneurysm rupture of the left ventricle wall, one of the more severe complications of the early post-infarction period.

1. Introduction

Biodegradable polymeric hydrogels including alginate polysaccharide hydrogels are used in medicine as surgical implants [1, 2] in particular to prevent heart aneurysm in post-infarction period [3, 4] and to treat advanced chronic heart failure [5, 6], as fillers to eliminate bone defects [7, 8] and as dressings on deep infected wounds [9, 10]. Hydrogel based biomaterials are also used in clinical pharmacology as transport systems [11] for targeted delivery of drugs [12, 13] and cells [14, 15], for immobilization and proliferation of mammalian cells, and as injectable solutions and pastes with delayed gelation [2] but also for many other medical, veterinary and biological applications [16].

The rheological properties (i.e. mechanical resistance and viscoelastic properties) of hydrogels are important parameters for specific biological and medical applications [12] but also for developing new injectable biomaterials along the path of new medical device creation [17]. The stiffness of hydrogels has been reported to be a direct criterion for the differentiation of cell types [18–20]. For drug delivery, hydrogels should preferentially reduce in viscosity upon injection and undergo rapid recovery upon removal of the stress